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EXAMINER	
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ART UNIT	PAPER NUMBER
1632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/502,332	MALISSEN ET AL.	
	Examiner	Art Unit	
	Thaian N. Ton	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-64* is/are pending in the application.

4a) Of the above claim(s) *38,48-56 and 62-64* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-37, 39-47, 57-61* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *23 July 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 35-64 are pending; claims 38, 48-56, 62-64 are withdrawn; claims 35-37, 39-47, 57-61 are under current examination.

Information Disclosure Statement

The information disclosure statement filed 7/23/04 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Election/Restrictions

Applicant's election with traverse of Group I in the reply filed on 5/22/06 is acknowledged. The traversal is on the ground(s) that the Examiner's interpretation of the art of Sommers does not teach the claimed invention, because they teach no mature T cells were present in their transgenic animals, whereas in the instant invention shows an exaggerated TH2 cell differentiation. See page 2 of the Response, filed 5/22/06. Applicants request to examine the subject matter of Groups I and II (claims 35-37, 39-47 and 57-61) together. See page 3 of the Response.

These arguments are found to be partially persuasive with regard to rejoinder of Groups I-II, in view of Applicants' arguments. However, the restriction with regard to Groups III-XI is maintained for reasons set forth in the Restriction, mailed 4/20/06.

Claims 38, 48-56, 62-64 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected groups, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 5/22/06.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 35-37, 39-47, 57-61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

A transgenic mouse whose genome comprises a mouse LAT gene encoding a mouse LAT protein wherein the mouse LAT protein consists of SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), wherein the mouse is homozygous for said gene, and the mouse has a phenotype of increased TH2 cells.

The specification does not reasonably provide enablement for the breadth of the claims, which are directed to non-human animals have any mutated LAT gene coding for a mutant LAT protein, wherein the mutant LAT protein leads to exaggerated TH2 differentiation, cells isolated from said non-human animal. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the Invention. The claims are directed to a non-human animal having a mutated LAT gene coding for a mutant LAT protein, wherein said mutant

LAT protein leads to an exaggerated TH2 cell differentiation. In specific embodiments, the mutation contains a single mutation of the tyrosine corresponding to Y136 in the mouse LAT protein, wherein the animal is a mouse, wherein the mutation consists of the replacement of the tyrosine by a residue prevention of the "tyrosine-based" sequences with the SH2 domain of proteins. The claims are further directed to germ cells or somatic cells from said non-human animals.

Breadth of the claims. The breadth of the claims encompasses any non-human animal, as well as any mutation for the LAT protein with the phenotype of exaggerated TH2 cell differentiation. The claims encompass any cells (somatic or germ), without a particular phenotype, isolated from the animal.

Guidance of the Specification/The Existence of Working Examples. The specification teaches the production of homozygous mutant LAT^{Y136F} mice, wherein the tyrosine residue at amino acid position 136 of SEQ ID NO: 1 (the endogenous mouse sequence) was mutated to a phenylalanine. See page 13, Example 1. The specification teaches characterization of the phenotype of these mice, by isolation of CD4+ T cells and eosinophils. It was found that the mutant mice's CD4 T cells had high levels of IL-4 and IL-10 transcripts, when compared to wild-type CD4 T cells, which only had IL-2 and IFN-a transcripts which are expected for primary T cells. Thus, the specification teaches that the LAT Y135F mice's phenotype was the spontaneous development of a high frequency of T_H2 cells, which is not observed in wild-type mice. See pages 17-18, bridging ¶. The specification teaches that this phenotype is unexpected, because studies of other LAT knock in mice revealed that murine T cell development was completely blocked, and that their thymocyte development was arrested at the immature CD4- CD8- stage, where no mature T cells were present. See page 2, lines 1-10. Thus, given the guidance of the specification and working examples, one of skill in the art would not expect the instantly disclosed LAT Y136F mice to exhibit a phenotype of increased T_H2 cells.

State of the Art/Predictability of the Art. The breadth of the claims are directed to any non-human animal, having a mutated LAT gene coding for a mutant LAT protein with a phenotype of exaggerated TH2 cell differentiation. However, the state of the art teaches that it would be unpredictable to produce a transgenic animal with a predictable phenotype. This is because the art of transgenic animals has for many years stated that the unpredictability lies with the site or sites of integration of the transgene into the target genome. Transgenic animals are regarded to have within their cells cellular mechanisms which prevent expression of the transgene, such as DNA methylation or deletion from the genome (Kappell et al (1992) Current Opinion in Biotechnology 3, 549, col. 2, parag. 2). Mullins et al (1993) states that not all animals express a transgene sufficiently to provide a model for a disease as the integration of a transgene into difference species of animal has been reported to given divergent phenotypes (Mullins et al (1993) Hypertension 22, page 631, col. 1, parag. 1, lines 14-17). The elements of the particular construct used to make transgenic animals are held to be critical, and that they must be designed case by case without general rules to obtain good expression of a transgene; e.g., specific promoters, presence or absence of introns, etc. (Houdebine (1994) J. Biotech. 34, page 281). "The position effect" and unidentified control elements also are recognized to cause aberrant expression (Wall (1996) Theriogenology 45, 61, parag. 2, line 9 to page 62, line 3). Mullins et al.(1996) disclose that "the use of nonmurine species for transgenesis will continue to reflect the suitability of a particular species for the specific questions being addressed, bearing in mind that a given construct may react very differently from one species to another." (Mullins et al (1996) J. Clin. Invest. 98, page S39, Summary). Well-regulated transgenic expression is not frequently achieved because of poor levels or the complete absence of expression or leaky expression in non-target tissues (Cameron (1997) Molec. Biol. 7, page 256, col. 1 -2, bridg. parag.). Factors influencing low expression, or the lack their of, are not affected by copy

number and such effects are seen in lines of transgenic mice made with the same construct (Cameron (1997), Molec. Biol. 7, page 256, lines 3-9). These factors, thus, are copy number independent and integration site dependent, emphasizing the role the integration site plays on expression of the transgene (Cameron (1997), Molec. Biol. 7, page 256, lines 10-13). Further, Sigmund (2000) states that the random nature of transgene insertion, resulting founder mice can contain the transgene at a different chromosomal site, and that the position of the transgene effects expression, and thus the observed phenotype (Sigmund (2000) Arteroscler. Throm. Vasc. Biol. 20, page 1426, col. 1, parag. 1, lines 1-7). With regard to the importance of promoter selection, Niemann (1997) states that transgenic pigs made with different promoters regulating expression of a growth hormone gene give disparate phenotypes - one deleterious to the pig, the other compatible with pig health (Niemann (1997) Transg. Res. 7, page 73, col. 2, parag. 2, line 12 to page 73, col. 1, line 4).

While the intent is not to say that transgenic animals of a particular phenotype can never be made, the intent is to provide art taught reasoning as to why the instant claims are not enabled. Given such species differences in the expression of a transgene, particularly when taken with the lack of guidance in the specification for any transgenic non-human animal, whose genome comprises a mutant LAT gene coding for a mutant LAT protein, wherein the animal exhibits exaggerated TH2 cell differentiation, other than the exemplified transgenic mouse, it would have required undue experimentation to predict the results achieved in any one host animal comprising and expressing mutant LAT gene, the levels of the transgene product, the consequences of that product, and therefore, the resulting phenotype.

Furthermore, it is noted that one of skill in the art could not rely upon the state of the art with regard to changing any residue to produce a protein with the same function. The claims broadly encompass any mutation in the LAT gene to

produce a mutant protein that leads to an exaggerated TH2 cell differentiation. For example, the state of the art teaches that highly homologous enzymes can have completely different For example, **Seffernick** et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Furthermore, the art also teaches that even a single amino acid difference can completely change the function of an enzyme. Specifically, **Witkowski** et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Thus, one of skill in the art would not be able to predict the change of any particular amino acid residue and the resultant functional change in the mutant protein.

Although specific embodiments limit the mutation to a tyrosine residue, the specification fails to provide guidance for these claims, because the mutation of the tyrosine is in a position that "corresponds" to Y136 in the mouse LAT protein. The specification fails to provide specific guidance for which tyrosine residues in LAT sequences (from other species), other than the wild-type mouse sequence that would correspond to Y136.

Claim 46 is directed to the targeted insertion of the transgene, such that it is under control of the endogenous LAT regulatory sequences. However, targeted insertion at a specific genomic location is only predictable with regard to mouse ES cells. The specification provides no guidance to targeted insertion into the genome of animals, using cells other than mouse ES cells. This is because the state of the art is such that ES cell technology is generally limited to the mouse system at present, and that only "putative" ES cells exist for other species (see Moreadith *et al.*, **J. Mol. Med.**, 1997, p. 214, *Summary*). Note that "putative" ES cells lack a demonstration of the cell to give rise to germline tissue or the whole animal, a demonstration which is an art-recognized property of ES cells. Moreadith *et al.*

supports this observation as they discuss the historical perspective of mouse ES cells as follows:

"The stage was set-one could grow normal, diploid ES cells in culture for multiple passages without loss of the ability to contribute to normal development. Furthermore, the cells contributed to the development of gametes at a high frequency (germline competence) and the haploid genomes of these cells were transmitted to the next generation. Thus, the introduction of mutations in these cells offered the possibility of producing mice with a predetermined genotype."

Such a demonstration has not been provided by the specification or the prior or post-filing art with regard to the generation of any species of animal ES cells, other than the mouse, which can give rise to the germline tissue of a developing animal. In addition, prior to the time of filing, Mullins *et al.* (**Journal of Clinical Investigation**, 1996) report that "although to date chimeric animals have been generated from several species including the pig, in no species other than the mouse has germline transmission of an ES cell been successfully demonstrated." (page 1558, column 2, first paragraph). Accordingly, in view of the state of the art with regard to ES cells, and unpredictability in targeted insertion in the genome of cells other than mouse ES cells, it would have required undue experimentation for one of skill in the art to target insertion of the recited LAT transgene into the genome of any cell in order to produce any non-human transgenic animal.

The phenotype of the mice, taught by the specification, is an increase in TH2 cells, however the breadth of the claims recites "exaggerated TH2 cell differentiation". The breadth of this phenotype is not enabling, because the specification fails to show exaggerated TH2 cell differentiation. TH2 cells are a subset of T-helper cells that express specific markers, such as IL-3, 4, 5, 10, and 13 (see Kuby, Immunology, 1994, page 311, Table 13-2). The specification identifies TH2 cells, IL-4 and IL-10 (see p. 17, lines 22-24). These are indicative of TH2 cells, but not the differentiation of cells to TH2. There is no specific guidance provided in

the specification with regard to cells that are differentiating into TH2 cells, nor any particular markers that are tested to show that cells upon the differentiation continuum are present in the mutant mice. Thus, the claims are not enabling for the breadth of "exaggerated TH2 cell differentiation" because the guidance in the specification is only directed to the increase in TH2 cells.

The Amount of Experimentation Necessary. The claims encompass non-human animals, having mutated LAT genes from other species. However, the specification fails to teach these embodiments, and further, fails to provide specific guidance with regard to what the phenotype of the resultant animal would be. For example, although the specification teaches mice with a mutation in the endogenous mouse LAT gene, the specification does not teach transgenic mice whose genome comprises a transgene that encodes for a mutant pig LAT protein, wherein the mutant pig LAT protein leads to exaggerated TH2 cell differentiation. As shown above, one of skill in the art would not be able to rely upon the art for predictability with regard to the resultant phenotype of the transgenic non-human animal.

The claims further encompass both heterozygous and homozygous non-human animals, and specific embodiments claim that the non-human animal carries a "null allele" of the LAT gene (see claim 45). These claims are not enabled, because the specification fails to teach the phenotype of heterozygous non-human animals, or non-human animals that carry a null allele of the LAT gene. As stated above, the phenotype resulting from any particular mutation, as broadly claimed is not predictable. The specification only provides specific guidance for homozygous mice with regard to the phenotype of increased TH2 cells. There is no guidance or teachings with regard to the phenotype of heterozygous mice (or broadly, non-human animals) or mice (or non-human animals) with a null allele of the LAT gene. One of skill in the art would have to practice undue experimentation to determine a nexus between a resultant phenotype and the breadth of mutation(s) encompassed

by the claims. Thus, it is determined that only homozygous mice are enabled within the scope of the invention.

Accordingly, in view of the state of the art, with regard to the unpredictability in phenotype of transgenic animals, the breadth of the claims, which encompass any mutated LAT gene and any non-human animal comprising said mutated LAT gene, the state of the art which shows that mutations of even one residue of a sequence can vastly change the function of a resultant protein, that the lack of guidance or teachings provided by the specification with regard to the resultant phenotype of any transgenic non-human animal, other than a mouse whose genome comprises a mouse LAT gene encoding a mouse LAT protein wherein the mouse LAT protein consists of SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), and the mouse has a phenotype of increased TH2 cells, it would have required undue experimentation for one of skill in the art to make and use the claimed invention.

Written Description

Claims 35-37, 39-47, 57-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Vas-Cath Inc. v. Mahurkar 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that, "[A]pplicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." *Vas-Cath Inc. v. Mahurkar,* 19USPQ2d at 1117. The specification does not, "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." *Vas-cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

While the specification provides adequate written description for the protein encoded by SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), the specification fails to provide a written description for any other mutated LAT protein, that when used as instantly claimed, would result in the phenotype of exaggerated TH2 cell differentiation. The claims broadly encompass mutated genes from any animal species, with any particular mutation. Specific claims (see claim 36, for example) limit the mutation to the tyrosine Y136 in the mouse LAT protein, but the specification fails to provide specific guidance or description as to what position the mutation would be in any other species, other than mouse. Specific claims (claims 57-61) are directed to the mutated mouse gene, but fail to provide description for the sequence which corresponds to a wild-type sequence and contains a single mutation of the tyrosine Y136. The specification only provides description for SEQ ID NO:1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine. Thus, there is no particular indication that Applicants had possession of the claimed invention. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described by the specification, and which are not conventional in the art as of Applicants' effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient and relevant identifying characteristics, as it relates to the invention as a whole, such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. In the instant case, the claimed embodiments of mutant genes that encode for a mutant protein that lead to exaggerated TH2 cell differentiation, from any species of animal, mutant LAT proteins that correspond to a wild-type sequence and contain mutations that "correspond to" the specific residue 136 in the mouse LAT protein, and mutated mouse genes that "correspond to" a wild-type sequence and contain a single mutation of the tyrosine 136 residue, lack a

written description. The specification fails to describe which mutated LAT proteins, other than the mouse LAT protein encoded by SEQ ID NO: 1, wherein the tyrosine at amino acid residue 136 has been substituted with phenylalanine (Y136F), would fall into the broadly claimed genus, which, when constructed and used as claimed, would result in the functional phenotype of exaggerated TH2 cell differentiation, as instantly claimed. The skilled artisan could not envision the detailed chemical structure of all of the mutant LAT genes encompassed by the claims, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention, and a reference to a potential method of isolating it. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what one has not conceived. See *Fiddes v. Baird,* 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGFs were found to be unpatentable due to lack of written description for that broad class. The specification only provided the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description of 35 U.S.C. 112 is severable from its enablement provision [see p. 1115].

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36, 37, 42-44, 47, 58-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36 and 57 contains the phrase "corresponds to a wild-type sequence". Claim 60 recites that the sequence "corresponds to" SEQ ID NO: 1. The metes and bounds of the term "corresponds to" cannot be readily determined because the phrase has various definitions. The definition of corresponding is found at http://www.thefreedictionary.com/corresponding (The Free Dictionary by Farlex [online], term "corresponding" [retrieved on 7/31/06]. Retrieved from the Internet,:URL: http://www.thefreedictionary.com/corresponding?p>) has definitions that indicate the term can mean related to, connected to, associated to, and similar in position or purpose. Given the multiple definitions in the art, and the lack of a definition of "corresponds to" in the specification, the metes and bounds of the claim are not clear. Claims 37, 43, 44 depend from claim 36; claims 58-61 depends from claim 57.

Adj. 1. corresponding - accompanying; "all rights carry with them corresponding responsibilities"

related, related to - being connected or associated; "painting and the related arts"; "school-related activities"; "related to micelle formation is the...ability of detergent actives to congregate at oil-water interfaces"

2. corresponding - similar especially in position or purpose; "a number of corresponding diagonal points"

similar - marked by correspondence or resemblance; "similar food at similar prices"; "problems similar to mine"; "they wore similar coats"

3. corresponding - conforming in every respect; "boxes with corresponding dimensions"; "the like period of the preceding year"

comparable, like

same - closely similar or comparable in kind or quality or quantity or degree; "curtains the same color as the walls"; "two girls of the same age"; "mother and son have the same blue eyes"; "animals of the same species"; "the same rules as before"; "two boxes having the same dimensions"; "the same day next year"

4. corresponding - agreeing in amount, magnitude, or degree; "the figures are large but the corresponding totals next year will be larger"

in proportion to, proportionate

commensurate - corresponding in size or degree or extent; "pay should be commensurate with the time worked"

Claim 42 recites the limitation "said mutation" in line 1; "the tyrosine" in line 2 and "the "tyrosine based sequences" in line 3 of the claim. There is insufficient antecedent basis for these limitations in the claim. The claim is also indefinite, because the metes and bounds of association of the "tyrosine-based sequences" cannot be determined. In particular, it is unclear what the quotation marks intend to encompass, for example, do they mean to just be limited to tyrosine sequences, or sequences with modifications that are "tyrosine-based."?

Claim 47, as written is unclear. The claim recites "any progeny thereof" in line 2 of the claim. It is unclear if this refers to progeny of the germ/somatic cell, or progeny of the non-human animal. Appropriate correction is requested.

Claims 58 and 59 are unclear. They both recite "said mutation" but it is unclear if this mutation relates to the single mutation or composite mutation recited in claim 57.

Claim 60 is unclear. The claim recites "the sequence corresponds to Sequence ID No. 1" in line 1 of the claim. The claim depends from claim 57, which recites two sequences, a mutant sequence, and a wild-type sequence. It is unclear if "the sequence" refers to the mutant sequence, or the wild-type sequence. Appropriate correction is requested. Claim 61 is similarly unclear, because it recites "the sequence contains exon 7 of the mutated gene."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 47 and 57-61 are rejected under 35 U.S.C. 102(a) as being anticipated by Sommers *et al.* (**J. Exp. Med**, 194(2), 135-142, cited in the prior Office action).

The claims are directed to a germ cell or somatic cell from a non-human animal having a mutated LAT gene coding for a mutant LAT protein, wherein said mutant LAT protein leads to an exaggerated TH2 cell differentiation. Further embodiments are directed to a mutated mouse gene coding for a mutant LAT protein, the sequence of which corresponds to a wild-type sequence and contains a single mutation of the tyrosine Y136 or a composite mutation of the three distal tyrosine residues, wherein the mutation consists of a tyrosine by phenylalanine. Note that the claims which recite that the sequence "corresponds to", see also rejection under §112, 2nd paragraph, and thus, any nucleic acid would "correspond" to a wild-type sequence.

Sommer *et al.* teach the generation of transgenic mice which have knock-in mutations of the four distal tyrosine residues of the LAT protein at positions 136, 175, 195 and 235. They particularly teach the mutation of these tyrosine residues to phenylalanine residues (see page 137, 1st ¶). They teach isolation of thymocytes from the mice (p. 137, 2nd column). The claims are directed to cells (claim 47) and mutated mouse genes (claims 57-61), none of which will have the phenotype of the non-human animal (exaggerated TH2 cell differentiation). Thus, Sommers *et al.* provide sufficient teachings to anticipate the claimed invention, because they teach cells isolated from mice with a mutated LAT gene coding for a mutant LAT protein, and they teach a mutated mouse gene coding for a mutant LAT protein that contains the Y136F mutation encompassed by the claims. With regard to claim 61, because they teach the mutation of the Y136 reside, it would inherently contain exon7 of the mutated gene. Accordingly, Sommers *et al.* anticipate the claimed invention.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Thaian N. Ton whose telephone number is (571) 272-0736. The Examiner can normally be reached on Monday through Thursday from 7:00 to 5:00 (Eastern Standard Time). Should the Examiner be unavailable, inquiries should be directed to Ram Shukla, SPE of Art Unit 1632, at (571) 272-0735. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the Official Fax at (571) 273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

thaian ton

Thaian N. Ton
Patent Examiner
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